WHAT IS CLAIMED IS:

1. A humanized immunoglobulin comprising a humanized heavy chain and a humanized light chain:

(1) the humanized light chain comprising three complementarity determining regions (CDR1, CDR2 and CDR3) having amino acid sequences from the corresponding complementarity determining regions of a mouse 21-6 immunoglobulin light chain, and a variable region framework from a human kappa light chain variable region framework sequence except in at least one position selected from a first group consisting of L45, L49, L58 and L69, wherein the amino acid position is occupied by the same amino acid present in the equivalent position of the mouse 21-6 immunoglobulin light chain variable region framework; and

(2) the humanized heavy chain comprising three complementarity determining regions (CDR1, CDR2 and CDR3) having amino acid sequences from the corresponding complementarity determining regions of a mouse 21-6 immunoglobulin heavy chain, and a variable region framework from a human heavy chain variable region framework sequence except in at least one position selected from a group consisting of H27, H28, H29, H30, H44, H71, wherein the amino acid position is occupied by the same amino acid present in the equivalent position of the mouse 21-6 immunoglobulin heavy chain variable region framework;

wherein the immunoglobulin specifically binds to a VLA-4 ligand with a binding affinity having a lower limit of about 10^7 M^{-1} and an upper limit of about five-times the binding affinity of the mouse 21-6 immunoglobulin.

2. The humanized immunoglobulin of claim 1 wherein the humanized light chain variable region framework is from an RE1 variable region framework sequence except in at least one position selected from the first group, and except in at least one position selected from a third group consisting of positions L104, L105 and L107, wherein the amino acid position is occupied by the same amino acid present in the equivalent

position of a kappa light chain from a human immunoglobulin other than RE1.

3. The humanized immunoglobulin of claim 2, wherein the humanized heavy chain variable region framework is from a 21/28'CL variable region framework sequence.

4. The humanized immunoglobulin of claim 3, wherein the humanized light chain variable region framework comprises at least three amino acids from the mouse 21.6 immunoglobulin at positions in the first group and three amino acids from the kappa light chain from the human immunoglobulin other than REI at positions in the third group, and the humanized heavy chain variable region framework comprises at least five amino acids from the mouse 21.6 immunoglobulin at positions in the second group.

5. The humanized immunoglobulin of claim 4, wherein the humanized light chain variable region framework is identical to the RE1 light chain variable region framework sequence except for the at least three positions from the first group and the three positions from the third group, and the heavy chain variable region framework is identical to the 21/28'CL heavy chain variable region framework sequence except for the at least five positions from the second group.

6. The humanized immunoglobulin of claim 5, wherein the at least three positions from the first group are positions L45, L58 and L69, and at the least five positions from the second group are positions H27, H28, H29, H30 and H71.

7. The humanized immunoglobulin of claim 6, wherein the humanized light chain comprises complementarity determining regions that are identical to the corresponding complementarity determining regions of the mouse 21-6 heavy chain, and the humanized heavy chain comprises complementarity determining regions that are identical to the corresponding complementarity determining regions of the mouse 21-6 heavy chain, except that

the CDR3 region of the humanized heavy chain may or may not comprise a phenylalanine residue at position H98.

8. The humanized immunoglobulin of claim 7, wherein the CDR3 of the humanized heavy chain comprises a phenylalanine residue at position H98.

9. The humanized immunoglobulin of claim 1, wherein the amino acid sequence of the mature light chain variable region is the sequence designated La (SEQ ID NO:7) in Fig. 6.

10. The humanized immunoglobulin of claim 1, wherein the amino acid sequence of the mature light chain variable region is the sequence designated Lb (SEQ ID NO:8) in Fig. 6.

11. The humanized immunoglobulin of claim 1, wherein the amino acid sequence of the mature heavy chain variable region is the sequence designated Ha (SEQ ID NO:11) in Fig. 7.

12. The humanized immunoglobulin of claim 1, wherein the amino acid sequence of the mature heavy chain variable region is the sequence designated Hb (SEQ ID NO:12) in Fig. 7.

13. The humanized immunoglobulin of claim 1, wherein the amino acid sequence of the mature heavy chain variable region is the sequence designated Hc (SEQ ID NO:13) in Fig. 7.

14. The humanized immunoglobulin of claim 9, wherein the amino acid sequence of the mature heavy chain variable region is Ha (SEQ ID NO:11) in Fig 7.

15. The humanized immunoglobulin of claim 9, wherein the amino acid sequence of the mature heavy chain variable region is Hb (SEQ ID NO:12) in Fig 7.

16. The humanized immunoglobulin of claims 9, wherein the amino acid sequence of the mature heavy chain variable region is designated Hc (SEQ ID NO:13) in Fig. 7.

17. A binding fragment of the humanized immunoglobulin of claim 14 or claim 16.

18. A humanized immunoglobulin of claim 14 or 16 that has a constant region domain.

19. A humanized immunoglobulin of claim 18, wherein the constant region domain has an effector function.

20. A humanized immunoglobulin of claim 18 wherein the constant region domain lacks an effector function.

21. The humanized immunoglobulin of claim 19, wherein the effector function is capable of complement fixation or antibody dependent cellular toxicity.

22. A nucleic acid encoding a heavy chain of a humanized antibody of claim 1 or a binding fragment thereof.

23. A nucleic acid encoding a light chain of a humanized antibody of claim 1 or a binding fragment thereof.

24. A computer programmed to display a three-dimensional representation of a humanized immunoglobulin of claim 1 on a monitor.

25. A pharmaceutical composition comprising a humanized antibody of claim 14 or 16, or a binding fragment thereof, and a pharmaceutically acceptable carrier therefor.

26. A method for detecting VLA-4 antigen, the method comprising:

administering a humanized immunoglobulin of claim 14 or 16, or a binding fragment thereof, to a patient or a tissue sample therefrom; and

detecting complexes formed by specific binding between the antibody or fragment and VLA-4 present in the target sample.

27. A method of inhibiting adhesion of a leukocyte to an endothelial cell, the method comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 25.

28. The method of claim 27, wherein the endothelial cell is a brain cell.

29. A method of treating an inflammatory disease in a patient comprising administering to the patient a therapeutically effective amount of the pharmaceutical composition of claim 25.

30. The method of claim 29 wherein the inflammatory disease is multiple sclerosis.